

(2) Copy of the currently pending claims, incorporating the amendments made herein;

(3) Marked-up version of the specification and claims showing the amendments made herein;

(4) Information Disclosure Statement and Form PTO-1449.

AMENDMENTS

In the specification:

Please replace the paragraph beginning on page 3, line 9 with the following rewritten paragraph:

B ~~MM~~One lipophilic derivative of MDP is N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine (MTP-PE). This muramyl tripeptide includes phospholipid tails that allow association of the hydrophobic portion of the molecule with a lipid environment while the muramyl peptide portion associates with the aqueous environment. Thus, the MTP-PE itself is able to act as an emulsifying agent to generate stable oil-in-water emulsions. MTP-PE has been used in an emulsion of 4% squalene with 0.008% TWEEN 80®, termed MTP-PE-LO (low oil), to deliver the herpes simplex virus gD antigen with effective results (Sanchez-Pescador et al., *J. Immunol.* (1988) 141:1720-1727), albeit poor physical stability. Recently, MF59, a safe, highly immunogenic, submicron oil-in-water emulsion which contains 4-5% w/v squalene, 0.5% w/v TWEEN 80®, 0.5% SPAN 85®, and optionally, varying amounts of MTP-PE, has been developed for use in vaccine compositions. See, e.g., Ott et al., "MF59 -- Design and Evaluation of a Safe and Potent Adjuvant for Human Vaccines" in *Vaccine Design: The Subunit and Adjuvant Approach* (Powell, M.F. and Newman, M.J. eds.) Plenum Press, New York, 1995, pp. 277-296. ~~MM~~

B Please replace the paragraph beginning on page 6, line 5 with the following rewritten paragraph:

B ~~MM~~ In another embodiment, the invention is directed to a composition comprising (a) a submicron oil-in-water emulsion which comprises 4-5% w/v squalene, 0.25-0.5%

B2 w/v TWEEN 80®, and 0.5% w/v SPAN 85®, and optionally, N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine, and (b) a selected antigen entrapped in, or adsorbed to, a biodegradable microparticle. ~~AM~~

Please replace the paragraph beginning on page 22, line 33 with the following rewritten paragraph:

B3 ~~W~~ Emulsifying agents suitable for use in the oil-in-water formulations include, without limitation, sorbitan-based non-ionic surfactants such as those commercially available under the name of SPAN® or ARLACEL®; polyoxyethylene sorbitan monoesters and polyoxyethylene sorbitan triesters, commercially known by the name TWEEN®; polyoxyethylene fatty acids available under the name MYRJ®; polyoxyethylene fatty acid ethers derived from lauryl, acetyl, stearyl and oleyl alcohols, such as those known by the name of BRIJ®; and the like. These substances are readily available from a number of commercial sources, including ICI America's Inc., Wilmington, DE. These emulsifying agents may be used alone or in combination. The emulsifying agent will usually be present in an amount of 0.02% to about 2.5% by weight (w/w), preferably 0.05% to about 1%, and most preferably 0.01% to about 0.5. The amount present will generally be about 20-30% of the weight of the oil used. ~~W~~

Please replace the paragraph beginning on page 25, line 9 with the following rewritten paragraph:

B4 ~~W~~ Particularly preferred submicron oil-in-water emulsions for use herein are squalene/water emulsions optionally containing varying amounts of MTP-PE, such as the submicron oil-in-water emulsion known as "MF59" (International Publication No. WO 90/14837; Ott et al., "MF59 -- Design and Evaluation of a Safe and Potent Adjuvant for Human Vaccines" in *Vaccine Design: The Subunit and Adjuvant Approach* (Powell, M.F. and Newman, M.J. eds.) Plenum Press, New York, 1995, pp. 277-296). MF59 contains 4-5% w/v Squalene (e.g., 4.3%), 0.25-0.5% w/v TWEEN 80®, and 0.5% w/v SPAN 85® and optionally contains various amounts of MTP-PE, formulated into submicron particles